

2009 NIEHS Biennial Advisory Council Report Certifying Compliance with Inclusion Guidelines

Overall Assurance for Compliance with Inclusion Guidelines

The 2009 Biennial Advisory Council Report Certifying compliance with Inclusion guidelines was presented to the National Advisory Environmental Health Sciences Council on February 19.

Information Regarding Aggregate Tracking and Inclusion Data

Prior to 2002, human subjects were reported in a single table format using the following racial categories: American Indian/Alaska Native; Asian; Black or African American; Hispanic or White. Following the 2000 census, GAO changed the reporting format. Under the current guidelines, investigators are required to ask subjects to identify ethnicity and race in a two question format: ethnicity first, followed by identification of race. Although the PI is expected to collect race and ethnicity data appropriate for their particular study, they must be able to report this data in the required NIH categories. Ethnicity is broken out as either Hispanic or Not Hispanic. Race must be broken out as American Indian/Alaska Native; Asian; Black or African American; Hawaiian/Pacific Islander; or White. Subjects may identify one or more races or they may decline to identify their race. If a subject identifies as being of two or more races, the subject is reported as "More than one race." If a subject declines to identify their race, the subject is reported as "Unknown/not reported." Studies funded prior to FY 2002 may use the new method of reporting only if the information on ethnicity is available. Both formats appear in the tables in the appendix. However, the number of studies using the old format continues to decrease. In FY 2005 and FY 2006, 73.8% and 94.4%, respectively, were reported using new format. As of FY2007 NIEHS no longer has any protocols reporting using the old format.

Table 1. FY 2007 Aggregate Enrollment Data for All Extramural Research Protocols

As of data submitted in FY2007, NIEHS no longer has any extramural projects reporting through the OLD format.

New Form: Total of All Subjects Reported Using the 1997 OMB Standards									Number of Protocols with Enrollment Data: 90			
	Total of All Subjects by Race								Total of All Subjects by Ethnicities			
	American Indian/Alaska Native	Asian	Black or African American	Hawaiian/Pacific Islander	White	More Than One Race	Unknown/Not Reported	Total	Not Hispanic	Hispanic or Latino	Unknown/Not Reported	Total
Female	1,103	7,876	5,599	78	21,953	1,373	1,954	39,936	33,034	5,646	1,256	39,936
	2.76%	19.72%	14.02%	0.2%	54.97%	3.44%	4.89%	58.08%	82.72%	14.14%	3.15%	58.08%
Male	780	5,739	3,085	47	15,934	1,330	1,828	28,743	23,709	4,501	533	28,743
	2.71%	19.97%	10.73%	0.16%	55.44%	4.63%	6.36%	41.8%	82.49%	15.66%	1.85%	41.8%
Unknown	16	3	9	1	17	1	38	85	27	40	18	85
	18.82%	3.53%	10.59%	1.18%	20%	1.18%	44.71%	0.12%	31.76%	47.06%	21.18%	0.12%
Total	1,899	13,618	8,693	126	37,904	2,704	3,820	68,764	56,770	10,187	1,807	68,764
	2.76%	19.8%	12.64%	0.18%	55.12%	3.93%	5.56%	100%	82.56%	14.81%	2.63%	100%

Table 2. FY 2008 Aggregate Enrollment Data for all Extramural Research Protocols

New Form: Total of All Subjects Reported Using the 1997 OMB Standards									Number of Protocols with Enrollment Data: 115			
	Total of All Subjects by Race								Total of All Subjects by Ethnicities			
	American Indian/ Alaska Native	Asian	Black or African American	Hawaiian/ Pacific Islander	White	More Than One Race	Unknown/ Not Reported	Total	Not Hispanic	Hispanic or Latino	Unknown/ Not Reported	Total
Female	1,416	8,858	6,611	133	39,290	2,063	4,674	63,045	43,264	11,814	7,967	63,045
	2.25%	14.05%	10.49%	0.21%	62.32%	3.27%	7.41%	58.95%	68.62%	18.74%	12.64%	58.95%
Male	1,067	6,034	3,820	79	27,851	2,044	2,913	43,808	31,423	8,760	3,625	43,808
	2.44%	13.77%	8.72%	0.18%	63.58%	4.67%	6.65%	40.96%	71.73%	20%	8.27%	40.96%
Unknown	16	3	9	1	20	1	47	97	30	43	24	97
	16.49%	3.09%	9.28%	1.03%	20.62%	1.03%	48.45%	0.09%	30.93%	44.33%	24.74%	0.09%
Total	2,499	14,895	10,440	213	67,161	4,108	7,634	106,950	74,717	20,617	11,616	106,950
	2.34%	13.93%	9.76%	0.2%	62.8%	3.84%	7.14%	100%	69.86%	19.28%	10.86%	100%

In FY2007 the total number of clinical research protocols in which subjects were enrolled (Table 1) was 90 with a total enrollment of 68,764 subjects. Of these, 39,936 (58.08%) were female; 28,743 (41.8%) were male and 85 (0.12%) chose not to identify their gender. The racial distribution was 2.76% American Indian/Alaska Native; 19.8% Asian; 12.64% Black or African American; 0.18% Hawaiian/Pacific Islander; 55.12% White; 3.93% more than one race; and 5.56% did not identify their race. For ethnicity 82.56% were not Hispanic; 14.81% were Hispanic; and 2.63% did not report their ethnicity.

In 2008 (Table 2), there were a total of 115 research protocols with a total enrollment of 106,950 subjects. Of these, 63,045 (58.05%) were female, 43,808 (40.96%) were male, and 97 (0.09%) chose not to report their gender. The racial distribution was 2.34% American Indian/Alaska native; 13.93% Asian; 9.76% Black or African American; 0.2% Hawaiian/Pacific Islander; 62.8% White; 3.84% more than one race; and 7.14% not reported. For ethnicity 69.86% identified as Not Hispanic; 19.28% identified as Hispanic or Latino; and 10.86% did not identify their ethnicity. There is a significant increase in the number of persons not identifying their ethnicity. This appears primarily to be due to an increase in studies focused on Latino populations. In many of these studies the subjects identify themselves only as Latino. These subjects do not identify Latino as an ethnicity with a separate racial identify. As studies have moved from reporting in the old format, where Hispanic/Latino was a race, there has been a steady increase in the numbers of unknown/not reported race in Hispanic populations. NIEHS staff continues to work with principal investigators in an effort to educate them on the importance of gender and race/ethnicity reporting to minimize discrepancies due to reporting errors by principal investigators.

The enrollment numbers that are reported each year are variable as studies end and new ones begin. It is important to note there was a significant increase in the reported numbers of enrolled subjects for NIEHS between 2007 and 2008. However, this sizeable increase was seen across all of NIH between 2007 and 2008. Therefore, NIH is investigating the phenomenon. For NIEHS the increase can be explained, at least in

part, to several factors: there was an overall increase of 28% in the number of protocols reporting subject enrollment, many of these are large population-based studies and the studies that ended tended to be smaller.

NIEHS continues to have more females than males represented in research protocols. In FY2007 there were 14 studies with females only and three studies with males only. In FY2008 there were 16 female only studies and two male only studies. In addition to the increase in the number of female only and decrease in male only studies in between FY2007 and FY2008, NIEHS has several mother/child epidemiology studies, which further increases the ratio of females to males.

With the development of the new Population Tracking System, it is now possible to identify the number of research protocols that are being performed in foreign countries. In FY 2007 (Table 3) 14.4% of the protocols with enrollment take place in foreign countries. That percentage increased in FY2008 to 19.13% (Table 4).

Table 3. FY2007 - Summary of all NIEHS Extramural Clinical Research including Phase III Trials Reported: Total Number of Protocols and Enrollment by Domestic versus Foreign Protocols

PROTOCOLS REPORTED	Total All Clinical Studies*	Domestic	%	Foreign	%
Protocols with Enrollment	90	77	85.6%	13	14.4%
%	55.6%	57.5%		46.4%	
Protocols with zero enrollment. Enrollment data has not yet been submitted	72	57	79.2%	15	20.8%
	44.4%	42.5%		53.6%	
Total Number of Protocols	162	134	82.7%	28	17.3%
%	100.00%	100.00%		100.00%	

Table 4. FY2008 - Summary of all NIEHS Extramural Clinical Research including Phase III Trials Reported: Total Number of Protocols and Enrollment by Domestic versus Foreign Protocols

PROTOCOLS REPORTED	Total All Clinical Studies*	Domestic	%	Foreign	%
Protocols with Enrollment	115	93	80.87%	22	19.13%
%	58.97%	0.6		0.55	
Protocols with zero enrollment. Enrollment data has not yet been submitted	80	62	77.50%	18	22.50%
	41.03%	0.4		0.45	
Total Number of Protocols	195	155	79.49%	40	20.51%
%	100.00%	100.00%		100.00%	

NIEHS continues to have few extramurally funded Phase III trials. Our last Phase III trial with enrollment ended in FY2005. That study, which took place in Mexico, examined the effect of dietary supplements containing calcium on bone lead resorption in pregnant mothers and the blood lead levels in their babies providing the first evidence that calcium supplementation suppresses the maternal-fetus/lactating infant transfer of lead as observed in the context of a large double-blind randomized clinical trial.

In FY2008 we funded two grants that have three Phase III trials between them. The first is an intervention study in Nepal (n=4200) looking at the effect of cook stove replacement on acute respiratory illness and respiratory health of newborns and children up to 36 months of age before and after replacement. A second part of this includes the respiratory health of the intervention on family members (n=16,800) living in the same house as the children. Because this is a large study, to make sure we can adequately follow the progress of the child cohort we required the investigator report these two populations separately. Thus there are two protocols for this one grant. Because the study population is 100% Asia, there will be no analysis by race. However, the sample is sufficiently large that analysis by gender is planned.

The second study is looking at the effect of indoor particulate matter air pollution generated by wood stoves on asthmatic children in rural Montana. It is a small three-arm study: placebo control, air filters and replacement of stove with an EPA rated stove. The population in rural Montana is primarily white so again racial analysis will not be possible. Analysis by gender will take place, but the sample size may not be sufficiently large to yield significant results. Both of these grants were funded in FY2008 and will not report enrollment until FY2009.

NIEHS had no Phase III trials with enrollment in FY2007 or FY 2008. Therefore no tables for Phase III studies are provided at this time.

Strategies for Ensuring Policy Compliance with Inclusion Guidelines

In order to fulfill the congressional mandates on gender/minority tracking NIEHS extramural division has instituted procedures that are updated as necessary to ensure compliance.

It is NIEHS policy that no notice of grant award will be issued for an application that has human subjects requiring tracking unless the target and/or enrollment data have been reviewed for entry into the population tracking database.

The responsibility for compliance and tracking is vested in staff in various roles of extramural research administration. These staff members participate as appropriate throughout the process. Specifically:

- Scientific Review Administrators review coding of applications for involvement of human subjects.
- The application receives peer review with respect to meeting inclusion requirements.

- A Program Analyst reviews the tracking/inclusion information from the competing application or progress report to determine whether it is a study that requires NIH tracking or may be excepted using specific NIH guidelines; reviews for completeness and interfaces with PIs to obtain any clarification or form revisions; and forwards the data to the Health Science Administrator (HSA) for concurrence.
- The HSA reviews Analysts recommendations and reviews the projects for appropriate scientific representation of women and minorities and that the grantees are accruing a diverse population in a timely manner in accordance with their approved research plan.
- The HSA discusses any scientific issues needing further attention with the applicant.
- When the issues are resolved, the HSA forwards concurrence to the Analyst and forwards the acceptable plan to the Grants Management Specialist (GMS).
- The analyst is responsible for entering codes into the NIH grants data base; assures completeness and accuracy of the data entered; and approves the data in the tracking system.

If the study section determines a study is not in compliance with human subject's regulations or the applicant has not addressed the requirements in the application, a code is placed in the system that bars funding. Generally awards are not made until the bars-to-funding are resolved. However, it is possible to make conditional awards where no funds may be expended on human subjects research until all human subjects' issues are resolved. The bar-to-funding data can be found in Table 5.

Table 5. Extramural Research Awards: Bars-to-Funding and Resolutions

	2007	2008
Total Number of Awards	307	219
Number of Awards Involving Human Subjects	102	76
	33.2%	34.7%
Number (%) of Awards Involving Human Subjects that met the Inclusion Requirements as Submitted	102	73
	100%	96.1%
Number (%) of Awards where <i>Minority-Only</i> Bar-To-Funding was Removed by Program Staff (M_U)	0	1
	0%	1.4%
Number of Awards where <i>Sex/Gender-Only</i> Bar-To-Funding was Removed by Program Staff (G_U)	0	0
	0%	0.0%
Number (%) of Awards where both Minority AND Sex/Gender Bar-To-Funding was Removed by Program Staff	0	2
	0.0%	.2.6%
Total Number (%) of Awards where Bar-To-Funding was Removed	0	3
	0.0%	3.9%

In FY 2007, 102 of the 307 applications funded had human subjects with no application having issues that required a bar-to-funding. In FY2008, 76 of the 219 applications funded had human subjects, and 3 applications (3.9%) had issues that resulted in a bar-

to-funding. No human subjects' research was allowed to be performed until all issues were resolved and the bars were removed.

Staff Training on the Utilization of the Population Tracking System

A staff member of the Program Analysis Branch, Division of Extramural Research and Training, has been designated as the person responsible for monitoring the system and tracking as required. She has received training on the population tracking system and also participates in annual training on human subject's and bioethics-related issues through the NIH Staff Training in Extramural Programs (STEP) and other seminars. The analyst is the sole person authorized to approve data into the tracking system. She currently represents the Institute on the Gender/Minority Inclusion committee and the electronic Population Tracking Users Group and served for on the Human Subjects Protection Liaison Committee from its inception in FY2001 until its dissolution in early summer, 2008.

Additional Staff Training

NIEHS staff has participated in relevant training programs and activities including the updates offered through the Staff Training on Extramural Programs. In FY2007, the analyst responsibly for tracking inclusion, along with other Extramural staff members, completed an 8-week course on "Ethical and Regulatory Aspects of Clinical Research Training." Due to the location of the NIEHS in North Carolina, most of the staff views sessions by video-teleconference. A record of staff participation in training activities is kept through the Office of the Director of the NIEHS Division of Extramural Research and Training.

It should be noted again that this Institute has supported very few studies that would be termed Phase III clinical trials. Nevertheless, staff are expected and required to be familiar with and enforce all requirements for research involving human subjects, as defined by NIH/DHHS.

Additional information on NIH Inclusion policies, including the NIH Inclusion Committee's Comprehensive Reports can be found on the Office of Research on Women's Health at <http://orwh.od.nih.gov/inclusion.html>.